

to where or by whom it was first employed in these cases. As a student I merely heard of it in a general way, and I only learned its value in some cases from its effect on a patient of mine who brought me a renowned (in certain circles) and secret asthma-cure made up and sold by a chemist in Loanhead. This patient had been advised by a friend to try it, and it really practically cured him. It contained nothing but 20 grains of sodium iodide in each 'dose, with some flavouring matters, no stramonium, no belladonna, &c. There is no mention of iodine or iodides for treatment of asthma or bronchitis by Cogswell (1837) or by Boinet (1855), both of whom wrote treatises on the therapeutic uses of iodine and its compounds. Their use in asthma is pretty well known now; but it would certainly do no harm to draw attention to it in the special way you intend."

"From the time when he was the minister of Currie parish, at least, Principal Barclay had been subject to severe asthmatic seizures, which yielded for a time to residence on two occasions for some months in Egypt, but recurred later on, accompanied by bronchitis, which was very disabling while it lasted, but which only brought out more clearly in his case the physical and mental vigour of a robust and, on the whole, imperturbable character, tending to the optimistic under many adverse conditions, of which these purely personal ones were by no means the most distressing to him. 'I think my lungs must have been made of leather,' he said to me after having suffered for about 30 or 40 years in this way, when I told him that he had come through all these attacks with wonderfully sound organs. In the earlier periods of this almost life-long illness he was attended by Dr. Craig of Ratho, who had as his assistant at the time one of my best pupils, a very devoted and intelligent young man, long since dead, as is also Dr. Craig himself. They sent me on one occasion a prescription with the remark that the medicine indicated in it had been found of very great service in Dr. Barclay's asthma, but that neither of them could understand the rationale of the prescription. This was not very wonderful, as it was one of those excessively complicated instances of polypharmacy in which (*more Anglico*) 14 or 15 different and more or less active substances were combined in one inextricable blend, so as to defeat as far as possible all reasonable efforts to discover the *modus operandi* of any particular constituent. Yet it was a very favourable example of this particular kind of prescription, 'elegant' in its form ('to use the conventional word), and, as regards its effects, quite worthy of the great reputation of the late Dr. Jephson of Leamington, from whom it emanated as a purely personal compliment, after his retirement from practice on account of blindness. Dr. Barclay had met Dr. Jephson at the house of Sir Wm. Gibson Craig of Riccartoun, and this prescription, with a number of very shrewd and clear-sighted directions as to diet, rest, and general hygienic precautions, were the results of the one only conference with the great English physician of the Midlands. At my suggestion, but after his own thorough and philosophical method, Dr. Barclay thereupon commenced a series of experiments in his own person on all the separate ingredients in this prescription which could by any reasonable interpretation be supposed to be its active principles, not discontinuing the complex form, but substituting from time to time simpler and simpler combinations, until in the end it was conveyed to him, and through him to me, that *iodide of potassium* was the agent that in all probability contained the curative virtues of the entire prescription. This was for me at the time, as a young teacher of medicine, quite a new therapeutic fact, and from that time onwards I rarely omitted an opportunity of preaching iodide of potassium (as well as prescribing it) in bronchial affections, together with the lesson conveyed by the whole investigation as regards simplicity in therapeutics *versus* polypharmacy. Dr. Barclay retained his belief in this remedy to the end of his days, and used to take two or three grains of it three times a day as a potent factor in helping him through his attacks, though it could not intercept them entirely.<sup>1</sup>

Dr. Barclay died in 1873, being, I think, in his eighty-seventh year at the time. His death was in one sense sudden—that is, unexpected as to the precise moment (it was during a service in the College chapel and I had seen him immediately before), but the long struggle with an ever-recurring disease and with many and great personal anxieties had completely exhausted a physical constitution originally of great vigour and a mind which almost to the very last was receptive and intelligent as well as sympathetic in no ordinary degree."

In conclusion, and without further discussion, I commend these simple facts to the profession with a certain sense that they might well have been published long ago had it not been for a desire for greater completeness in setting forth what had, nevertheless, a powerful and abiding influence on my own practice at the time and since.

Edinburgh.

<sup>1</sup> "Although this is not a suitable place for further discussion of this subject I may be permitted to add that the properties here attributed to the iodides were quite unrecognised in the great work of Pereira, and, so far as I can discover, were unknown to the medical profession at large at the time of the incident here referred to. It is perhaps not easy to say how far the oral teaching above referred to may have indirectly influenced professional opinion, but the cardinal fact of the Rev. Dr. Barclay's logical analysis of Jephson's prescription has never been stated in print (so far as I know) until now."

**DEVON MEDICAL CHARITIES.**—The late Mrs. E. Taylor of Exeter bequeathed £1000 to the Devon and Exeter Hospital, £100 to the West of England Eye Infirmary, and £100 to the Exeter Dispensary.

**THE LATE PROFESSOR ALFRED HUGHES.**—Mrs. Hughes, the widow of the late Professor A. Hughes, has contributed £1000 towards the endowment of the Alfred Hughes Anatomical Museum at University College, Cardiff.

## RAT PLAGUE.

A PRELIMINARY COMMUNICATION ON AN OUTBREAK OF DISEASE IN RATS AT CAPE TOWN.

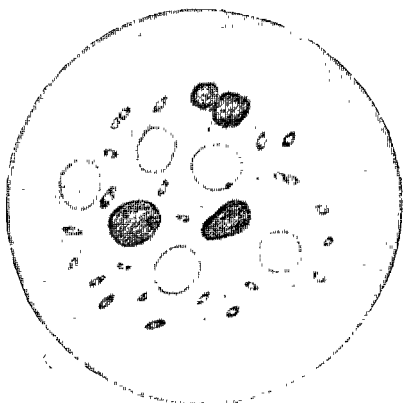
BY ALEXANDER EDINGTON, M.D., F.R.S. EDIN.,  
DIRECTOR OF THE COLONIAL BACTERIOLOGICAL INSTITUTE,  
CAPE COLONY.

ON Feb. 5th I arrived from England at Cape Town, *en route* to Port Elizabeth. At Cape Town I was informed by the Honourable the Colonial Secretary that it had been reported to him that rats were dying in great numbers from bubonic plague. He accordingly thought proper to detain me at Cape Town in order to investigate the matter. Accounts from reliable persons went to show that rats had been dying in the south arm of the docks. Instructions were therefore issued to the police and others to procure for me specimens of infected rats either dead or alive. During the following six days, however, no rats were found and I was therefore forced to report that, so far, no evidence had been brought forward to show that rats were dying from plague. On the following day, however, a rat was found in the south arm which had just died and it was forwarded to me, while at the same time authority was given to me to proceed to the isolated station to which certain persons who were believed to be suffering from bubonic plague had been sent. On proceeding to the latter place I found 12 persons had been admitted, most of whom had very well-marked buboes either in the femoral or axillary regions. I opened into most of the buboes by means of a sterilised hypodermic syringe and in the material thus collected I was able to demonstrate the presence of the bacillus of bubonic plague in most instances. Cultivation experiments were also successfully carried out and since that date I have produced the disease by inoculation of the cultures in guinea-pigs and rabbits. It is, however, in connexion with the disease in rats that this communication has been made.

The rat sent to me as having recently died in the south arm of the docks was carefully examined. At the post-mortem examination which was made with the assistance of my colleague Mr. Duncan Hutcheon, M.R.C.V.S., the chief of the Colonial Veterinary Department, the following conditions were seen. The animal was well nourished. No fluid or exudation was seen in connexion with either the mouth, the eyes, or the nose. No subcutaneous hæmorrhages were noticed. There was an abundance of clear, yellow serum in the pleural cavity and the pericardium was filled with a similar fluid. The lungs were quite normal. The blood in the heart was still fluid and no pathological changes were observed in the heart. The peritoneum was normal. The liver was congested but showed no other change. The spleen was normal in size, colour, and consistence. The adrenals were enlarged and very pale in colour. No enlarged glands were found. The blood in the veins was fluid. On making a microscopic examination of the heart blood, axillary blood, and the spleen and liver juice, I found enormous numbers of bacteria. Their form was oval and frequently they were joined as diplobacteria. In size the longest segments, which, like the shorter forms, always had rounded ends, were  $3\mu$  in length and  $1.5\mu$  in breadth. The diplo-bacterial forms measured  $4\mu$  in length and  $1.2\mu$  in breadth, while the smaller single oval forms measured  $1.5\mu$  in length and  $1\mu$  in breadth. In preparations from the spleen which were stained by methyl violet simultaneously with preparations made from the buboes of the patients affected with plague, while in the latter the bacteria always showed well-marked bi-polar staining the rat bacteria did not show this reaction. Fig. 1 shows the form of the plague microbes as seen in the buboes, while Fig. 2 shows the forms of the rat bacterium. Fig. 3 shows a primary culture of the plague bacilli, while Fig. 4 shows a primary culture of the rat bacterium. These cultures were made, the rat on the evening of Feb. 11th and the plague microbe on the morning of Feb. 12th. The same batch of agar-agar was used and the examinations were made two days later. The culture of the rat microbe was much more profuse than that obtained from patients suffering from the plague. In the latter case only a few isolated colonies grew, while in the former the spleen gave an almost confluent mass of growth and the blood yielded discrete colonies.

The primary culture of the rat microbe presented the most remarkable forms: some were diplococci or diplo-bacteria, others formed single and longer segments, while others formed large cells the somewhat spherical form of which was irregular in conformation, staining affinities, and size. The latter observation, taken in conjunction with the results of microscopical examination of the organs and blood of the

FIG. 1.

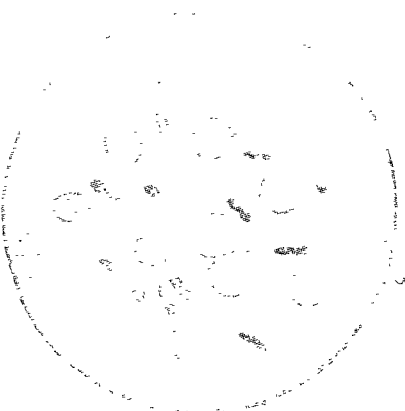


Pus from bubo of a Cape Town case of plague.

rat, caused me to declare, pending further experiments, that the disease in the rats was not identical with bubonic plague. On culture the rat microbe does not present any characteristic which would sufficiently distinguish it from bubonic plague. Moreover, in buttered bouillon it also forms stalactite growths. Inoculations of the bacilli obtained from the patients afflicted with Cape plague on litmus agar showed an acid reaction after eight days but the rat bacterium failed to show this.

After journeying to Grahamstown I proceeded to carry out experimental inoculations in animals with the cultures derived from the rat. In my inoculation experiments the

FIG. 2.



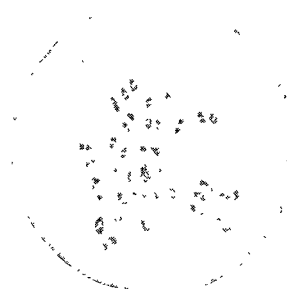
Juice from spleen of rat dead from rat plague.

following procedure was carried out for the purpose of preparing material for inoculation. A tube of alkaline bouillon was inoculated with a trace of an agar culture by means of a platinum needle, and after 24 hours' cultivation from five to 10 drops were used to inoculate animals by subcutaneous injection. Such a bouillon tube thus inoculated shows only a very slight turbidity after shaking and the quantity of the bacteria contained in five or 10 drops is, therefore, not large. On March 1st two guinea-pigs, Nos. 1 and 2, were each inoculated with 10 drops of a 24 hours' old bouillon culture. On the following day both seemed well, but on March 3rd both were very sick and No. 1 died on that day. The post-mortem examination was made almost at the moment of death. The eyes were bright and had a very slight watery discharge seen at the inner canthi. Under the skin of the right foreleg was found a small gland two millimetres in length and one millimetre in breadth. It was semi-transparent and seemed filled with a watery fluid. Almost the whole of the subcutaneous tissue, specially that on the ventral surface of the body, was occupied by a pale gelatinous oedema. On the left side was found a small area 10 millimetres in diameter, slightly hæmorrhagic in character. In the left groin two glands were found, very small in size, which were also oedematous, and when cut emitted a clear

fluid. The site of inoculation was enormously oedematous and the track of the needle was defined by a slight extravasation of blood. The oedema around and beneath this was absolutely clear and coagulated, being about six millimetres in thickness. This area of clear oedema was one and a half inches in length. The spleen was very slightly enlarged, being about 21 millimetres in length and 10 millimetres in breadth and two millimetres in its thickest part. In consistence it was firm and no abnormality otherwise was detected. One small gland was also found in the abdomen which was almost transparent. The liver was slightly congested, otherwise normal. Cultures made from the blood of the heart and the juice of the liver and the spleen allowed of my recovering the bacterium again in a state of purity. Examinations of the spleen pulp revealed innumerable bacteria. The whole looked like a pure culture.

On March 4th Guinea-pig No. 2 died. The post-mortem examination revealed similar conditions to that found in Guinea-pig No. 1, but certain additional features were also to be noticed. There was a small amount of fluid in the pericardium. The spleen was enlarged and covered all over with small white points similar to the condition which is found in guinea-pigs which have been inoculated with bubonic plague bacilli. One enlarged gland was found in the area of inoculation which was hyperæmic and opaque. Such glands as were found in other situations were semi-transparent as in the former cases.

FIG. 3.



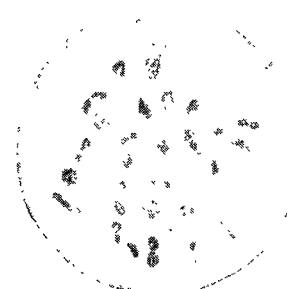
Primary culture from bubo of a Cape Town case of plague.

On March 4th a guinea-pig (No. 3) was inoculated with 10 drops of a 24 hours' old bouillon culture. On March 8th it died, and the post-mortem examination showed conditions similar to those found in Guinea-pig No. 2.

On March 5th a baboon was inoculated with 10 drops of the same culture as was used to inoculate Guinea-pig No. 3. The inoculation was made in the forearm. No swelling formed at the site of inoculation and no bubo formed in the axilla. It was never sick and to-day, three weeks later, it is in perfect health.

On March 7th two rabbits (Nos. 1 and 2) were each inoculated with 10 drops of a bouillon culture and a guinea-pig (No. 4) was inoculated with the same material and dose as control. On March 12th Guinea-pig No. 4 died and the post-mortem examination revealed similar lesions to those seen in Guinea-pigs Nos. 2 and 3. As the rabbits never showed the slightest signs of sickness they were re-inoculated

FIG. 4.



Culture from spleen of rat dead from rat plague. (Figs. 1 to 4, Zeiss, 2 mm. ap. and ocular 8).

on March 19th with 10 drops of a 24-hours bouillon culture of the bubonic plague bacilli which I had isolated from one of the Cape Town cases, and at the same time I inoculated one guinea-pig (No. 6) with the same dose for the purpose of control to this experiment. As this latter animal, however, struggled at the moment of inoculation a portion of

the material was ejected from the inoculation wound, so that the dose which it received must have been smaller than that which was injected in the first instance. On March 24th Rabbit No. 1 died. There was great sanguineous cedema at the site of inoculation involving several glands. There was some congestion of the larger bowel. The liver was enlarged, congested, and showed a number of small white points which were irregularly scattered here and there over it. These points were irregular in size, never exceeding a millimetre in diameter, many being smaller. The spleen was enlarged and discoloured, portions being reddish and parts, especially towards one end, greenish in colour. Several enlarged and hyperæmic glands were discovered. The lungs showed inflammation in patches and a small amount of fluid was found in the pericardium. Pure cultures of the bacilli were obtained from the spleen and liver. On the 25th Rabbit No. 2 died. The post-mortem examination revealed similar conditions as in Rabbit No. 1. The spleen showed a similar discolouration, while the white points in the liver were much more numerous. Cultures of the plague bacilli were also obtained from the spleen and blood in this case.

On March 26th Guinea pig No. 4 (control experiment) died. A great tumour was found at the site of the inoculation of a hæmorrhagic character involving several glands. The glands of the opposite side were also enlarged. A sanguineous effusion surrounded the site of inoculation and extended over the abdomen. The lungs were affected with broncho-pneumonia and there were numerous areas of actual necrosis. Some fluid was found in the pericardium, but small in amount. The liver was enlarged, congested, and had some small white points studded over it. These ranged in size from a pin-point to that of a pin-head. The spleen was enlarged and absolutely studded over its surface and throughout its substance with white points. On March 20th two rabbits (Nos. 3 and 4) and one guinea-pig (No. 7) were each inoculated with 10 drops of a 24 hours' old bouillon culture of the rat bacterium which had been passed through a guinea-pig. On March 25th the guinea-pig died. The lesions in this case were very well marked and of the characters seen in the former cases of guinea-pigs inoculated with this microbe. The spleen was enormously enlarged. The lungs were slightly inflamed in patches. On March 26th Rabbit No. 3 died from causes which could not be ascertained. The post-mortem examination was kindly made by Dr. W. Ramsay Smith, the President of the Central Board of Health of South Australia, and Mr. J. Desmond, the Government veterinary surgeon of the same State. I was very pleased to have the assistance of these gentlemen, since they have had in Australia a rather extended experience in regard to the pathology and bacteriology of plague. The site of inoculation was occupied by a dry abscess the pus of which was tough and tenacious. All the organs were healthy except the liver, which was affected by animal parasites. Microscopic examination failed to detect any bacteria at all and tubes of agar which were inoculated from the liver, spleen, and blood remained sterile.

On March 28th I killed the remaining rabbit. Here, as in the former case, the site of inoculation was occupied by an abscess the pus of which was equally tough and tenacious. The lungs were affected by numerous hydatids; otherwise every organ in the body was quite healthy.

On March 26th two pigeons were each inoculated with five drops of a 12 hours' old bouillon culture of the rat microbe. Unfortunately while the inoculation was being made in the second pigeon the needle pierced the skin at the farther point and thus almost the whole of the fluid passed out among the feathers and but a small dose could have been left under the skin. The point selected for inoculation was the front of the chest between the delicate skin and the pectoral muscles. On March 31st Pigeon No. 1 died. At the post-mortem examination a tumour was found between the thin integument and the muscular tissue below, and had also infiltrated the muscular substance itself. The heart was absolutely empty in the ventricles and only a trace of blood was found in the right auricle. The liver was very deeply congested. No other abnormality was detected. Examination of the blood and of the juice of the liver showed innumerable bacteria which, in the case of the liver, showed extremely well-marked bi-polar staining. Pigeon No. 2 died on the afternoon of April 1st. The post-mortem examination revealed almost identical lesions. Cultures made on agar from the blood and liver juice in both these cases gave plentiful and absolutely pure cultures of the rat microbe.

Since, therefore, we have in the rat a disease which is

communicable to guinea-pigs but not to rabbits, and to which rabbits are also refractory even after it has been passed through the guinea-pig; and since, moreover, inoculation of the rabbit with this rat bacterium in its virulent form gives no protection against a subsequent inoculation with bubonic plague, it seems clearly proved that this rat plague cannot be bubonic plague. The peculiar susceptibility of pigeons to the rat disease also indicates the difference between that malady and bubonic plague. In future steps will have to be taken in case of rats being affected with a disease simulating plague to inoculate other animals than guinea-pigs. My experiments show that the rabbit is probably the best animal to use in conjunction with guinea-pigs.

## ALCOHOL AND ARSENIC IN THE ETIOLOGY OF ALCOHOLIC NEURITIS.

BY E. FARQUHAR BUZZARD, M.B., M.R.C.P. LOND.,  
REGISTRAR TO THE NATIONAL HOSPITAL FOR THE PARALYSED  
AND EPILEPTIC.

THE recent epidemic of arsenical neuritis amongst the beer-drinkers of the northern and midland counties has led to the discussion of several interesting points in relation to peripheral neuritis in general and that form which is the result of alcoholism in particular. The word "alcoholism" is used advisedly, for we find that medical authorities are by no means agreed as to what particular constituent of alcoholic beverages is responsible for the lesions in the peripheral nerves of their consumers.

Among the most notable opinions that have recently been put forward and emphasised by eminent medical men are (1) that ethyl alcohol *per se* cannot produce neuritis; and (2) that "alcoholic neuritis" only occurs in beer-drinkers and not in pure spirit-drinkers. It has, moreover, been widely suggested (3) that alcoholic neuritis is really a misnomer and that the causal factor in those cases to which we have been accustomed to apply the name may yet be found in arsenic acting in inconsiderable doses. The first of these three theories—the one which denies to ethyl alcohol a selective pathological action on the peripheral neurons—is difficult to prove or to disprove. The second and third theories may reasonably be expected to stand or fall under the test of clinical experience and such other tests as experimental investigation may suggest.

With a view to elucidating the facts which clinical observation in a large number of cases can disclose the author of this paper has conducted a careful investigation of the notes on 120 of the most recent cases of "alcoholic" neuritis which are to be found in the case-books at the National Hospital for the Paralysed and Epileptic, Queen-square, London. The above number includes only those cases in which there seems to be no reasonable doubt that immoderate drinking was, at any rate, a possible etiological factor and does not include those in which some other toxic agent had been shown to be present, either alone or in conjunction with alcoholism. The cases occurred during the last 12 years and in that time about 20 other cases of multiple neuritis were treated in the hospital in which alcoholism was a possible but not a reliable cause. If we take all the cases of multiple neuritis for the period they can be classified thus to show their relative numerical strength.

Cases.		Cases.	
Alcohol ... ..	120	Post-influenzal ... ..	3
Alcohol (doubtful) ... ..	20	Lead ... ..	21
Alcohol and marked tuber- culosis ... ..	7	Malaria ... ..	3
Alcohol and septicæmia ... ..	2	Arsenic ... ..	2
Septicæmia alone ... ..	4	Post-typhoid ... ..	1
Post-diphtheritic ... ..	34	Diabetic ... ..	5
		Unknown cause ... ..	5

In the study of these notes especial attention has been paid to the following points: (1) age; (2) sex; (3) habits in reference to alcohol; (4) changes of a nutritional, vaso-motor, or pigmentary nature in the skin, hairs, or nails; and (5) the result of treatment with arsenical drugs.

1 and 2. *Age and sex of the patients.*—These two points may be briefly dismissed. Among 120 patients there were